long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency

Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency is a rare condition that prevents the body from converting certain fats to energy, particularly during periods without food (fasting).

Signs and symptoms of LCHAD deficiency typically appear during infancy or early childhood and can include feeding difficulties, lack of energy (lethargy), low blood sugar (hypoglycemia), weak muscle tone (hypotonia), liver problems, and abnormalities in the light-sensitive tissue at the back of the eye (retina). Later in childhood, people with this condition may experience muscle pain, breakdown of muscle tissue, and a loss of sensation in their arms and legs (peripheral neuropathy). Individuals with LCHAD deficiency are also at risk for serious heart problems, breathing difficulties, coma, and sudden death.

Problems related to LCHAD deficiency can be triggered by periods of fasting or by illnesses such as viral infections. This disorder is sometimes mistaken for Reye syndrome, a severe disorder that may develop in children while they appear to be recovering from viral infections such as chicken pox or flu. Most cases of Reye syndrome are associated with the use of aspirin during these viral infections.

Frequency

The incidence of LCHAD deficiency is unknown. One estimate, based on a Finnish population, indicates that 1 in 62,000 pregnancies is affected by this disorder. In the United States, the incidence is probably much lower.

Genetic Changes

Mutations in the *HADHA* gene cause LCHAD deficiency. The *HADHA* gene provides instructions for making part of an enzyme complex called mitochondrial trifunctional protein. This enzyme complex functions in mitochondria, the energy-producing centers within cells. As the name suggests, mitochondrial trifunctional protein contains three enzymes that each perform a different function. This enzyme complex is required to break down (metabolize) a group of fats called long-chain fatty acids. Long-chain fatty acids are found in foods such as milk and certain oils. These fatty acids are stored in the body's fat tissues. Fatty acids are a major source of energy for the heart and muscles. During periods of fasting, fatty acids are also an important energy source for the liver and other tissues.

Mutations in the *HADHA* gene that cause LCHAD deficiency disrupt one of the functions of this enzyme complex. These mutations prevent the normal processing of long-chain fatty acids from food and body fat. As a result, these fatty acids are not

converted to energy, which can lead to some features of this disorder, such as lethargy and hypoglycemia. Long-chain fatty acids or partially metabolized fatty acids may also build up and damage the liver, heart, muscles, and retina. This abnormal buildup causes the other signs and symptoms of LCHAD deficiency.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- 3-hydroxyacyl-CoA dehydrogenase, long chain, deficiency
- LCHAD deficiency
- long-chain 3-hydroxy acyl CoA dehydrogenase deficiency
- long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency
- long-chain 3-OH acyl-CoA dehydrogenase deficiency
- trifunctional protein deficiency, type 1

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Elevated C16-OH +/- C18:1-OH and Other Long Chain Acylcarnitines https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/C16-OH.pdf

Formal Treatment/Management Guidelines

- New England Consortium of Metabolic Programs: Acute Illness Protocol http://newenglandconsortium.org/protocols/acute_illness/fatty-acid-oxidation-disorders/LCHADD.pdf

Genetic Testing

- Genetic Testing Registry: Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency https://www.ncbi.nlm.nih.gov/gtr/conditions/CN074230/

Other Diagnosis and Management Resources

- Baby's First Test
  http://www.babysfirsttest.org/newborn-screening/conditions/long-chain-l-3-hydroxyacyl-coa-dehydrogenase-deficiency
- MedlinePlus Encyclopedia: Hypoglycemia
  https://medlineplus.gov/ency/article/000386.htm
- MedlinePlus Encyclopedia: Peripheral Neuropathy
  https://medlineplus.gov/ency/article/000593.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Hypoglycemia
  https://medlineplus.gov/ency/article/000386.htm
- Encyclopedia: Peripheral Neuropathy
  https://medlineplus.gov/ency/article/000593.htm
- Health Topic: Lipid Metabolism Disorders
  https://medlineplus.gov/lipidmetabolismdisorders.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- LCHAD deficiency
  https://rarediseases.info.nih.gov/diseases/6867/lchad-deficiency

Educational Resources

- Disease InfoSearch: LCHAD deficiency
  http://www.diseaseinfosearch.org/LCHAD+deficiency/4126
- Illinois Department of Public Health
  http://www.idph.state.il.us/HealthWellness/fs/mcad.htm
- MalaCards: lchad deficiency
  http://www.malacards.org/card/lchad_deficiency
- Merck Manual Professional Version
  http://www.merckmanuals.com/professional/pediatrics/inherited-disorders-of-metabolism/beta-oxidation-cycle-disorders#v25254053
- My46 Trait Profile
  https://www.my46.org/trait-document?trait=Long%20chain%203-Hydroxyacyl-CoA%20dehydrogenase%20deficiency&type=profile
- New England Consortium of Metabolic Programs
  http://newenglandconsortium.org/for-families/other-metabolic-disorders/fatty-acid-oxidation-disorders/lchadd/
- Orphanet: Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=5
- Screening, Technology, and Research in Genetics
  http://www.newbornscreening.info/Parents/fattyaciddisorders/LCHADD.html
- Virginia Department of Health
  http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet_LCHAD_English.pdf

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases (CLIMB)
  http://www.climb.org.uk
- Children's Mitochondrial Disease Network (UK)
  http://www.cmdn.org.uk/
- FOD (Fatty Oxidation Disorders) Family Support Group
  http://www.fodsupport.org/lchad.htm
- United Mitochondrial Disease Foundation
  http://www.umdf.org/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28long-chain+3-hydroxyacyl-CoA+dehydrogenase+deficiency%5BTIAB%5D%29+OR+%28LCHAD%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- LONG-CHAIN 3-HYDROXYACYL-CoA DEHYDROGENASE DEFICIENCY
  http://omim.org/entry/609016

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